

Figure 1. Percent platelet aggregation in patients on clopidogrel using different concentrations of adenosine diphosphate (ADP) and either citrate (open bars) or PPACK (solid bars) as anticoagulant. * $p < 0.05$.

dual antiplatelet therapy of clopidogrel and aspirin. The results demonstrate that citrate anticoagulated plasma undergoes markedly less platelet aggregation, which was significant at all concentrations of ADP tested. This is noteworthy because studies have suggested that there is a relationship between the degree of platelet inhibition and major adverse clinical events (5).

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Removal of Iodine Contrast From Coronary Sinus in Swine During Coronary Angiography

To the Editor: The use of contrast during coronary angiography (CA) in patients with renal disease is associated with a substantial risk of renal failure (30% to 50%). Previous studies have shown that the amount of contrast used during CA correlates with contrast-induced nephropathy (CIN) (1,2). Despite preventive care, CIN occurs with high frequency and is responsible for adverse outcomes (1,2). Most of the cardiac veins drain into the coronary sinus (CS). Anatomically, it should be possible to remove most of the contrast from the CS during CA using a catheter that can occlude the CS and remove blood distal to the occlusion. Commercially available CS catheters such as Heartport (Redwood City, California) (3) are safely used in the CS for cardioplegia or during biventricular pacing. In this study, the Heartport catheter was used to remove a mixture of blood and contrast from the CS during CA of five pigs.

Five fasted swine were sedated with atropine (0.05 mg/kg, intramuscular injection) and ketamine (20 mg/kg, intramuscular injection) and anesthetized with isoflurane. The ventilator settings were adjusted during the experiments to maintain normal partial oxygen pressure (PO_2) and partial carbon dioxide pressure (PCO_2).

The left main coronary artery was accessed from the left carotid artery using an 8-F multipurpose catheter. Standard techniques were used with back flush of the contrast during CA under fluoroscopy. Coronary angiography was performed after hand injection of 5 ml of a non-ionic iodinated contrast material (Omnipaque-350, Amersham Health Inc., Princeton, New Jersey).

The CS was engaged by using a Heartport catheter (Ethicon Inc., Cornelia, Georgia) (Fig. 1) via the external jugular vein and 11-F sheath. Immediately after coronary injection, the balloon at the tip of the catheter was inflated and CS blood was collected for 10 s (50 cc). Contrast injection and removal were repeated three times. The occlusion of CS did not affect CA interpretation.

The amount of contrast in the collected blood from the CS was quantified with high-performance liquid chromatography (samples were analyzed by Galbraith Laboratories, Knoxville, Tennessee) and a quantitative dual-energy technique developed in our laboratory. The University of California at Irvine Institutional Animal Care Committee approved this study.

We used a quantitative dual energy technique (4) for iodine mass determination. All images were acquired using a conven-

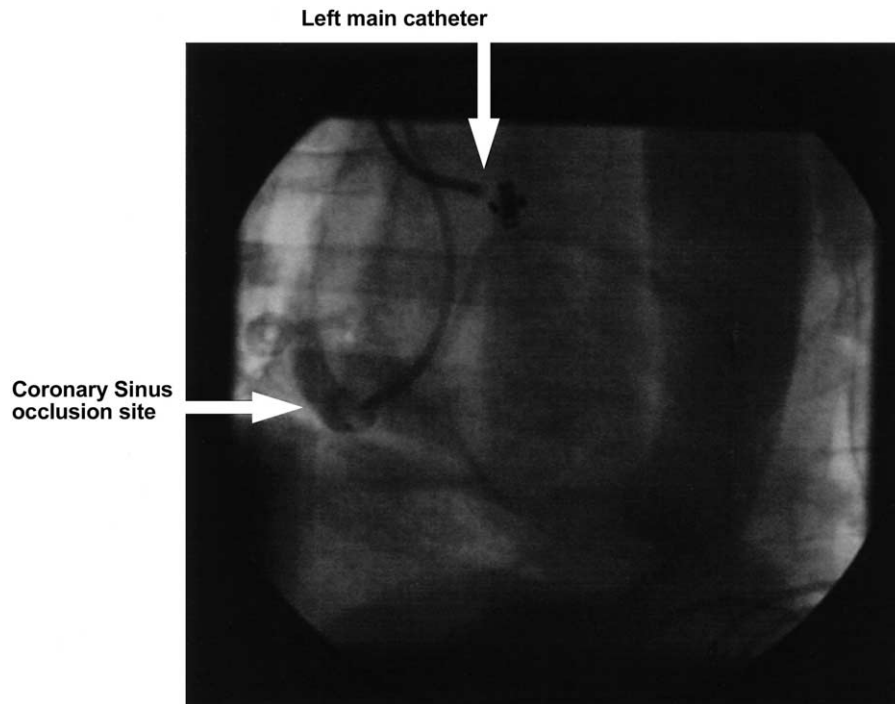


Figure 1. Simultaneous contrast injection into the left main coronary and occlusion of the coronary sinus showing contrast trapped in the coronary sinus before entering systemic circulation for removal (30° right anterior oblique view).

tional X-ray tube (Dynamax 79-45/120, Machlett Laboratories, Stamford, Connecticut), a constant potential X-ray generator (Optimus M200, Philips Medical Systems, Shelton, Connecticut), and a PaxScan 4030A flat panel detector (Varian Medical Systems, Salt Lake City, Utah). The syringes used to collect the blood samples were imaged over a step phantom with 7.50-cm, 9.25-cm, 11.00-cm, and 13.00-cm steps and an air gap of 10 cm between the phantom and detector. Low-energy images were acquired at 60 kVp and 6.0 mAs. High-energy images were acquired at 120 kVp and 5.0 mAs with an added 0.8-mm thick 925 sterling silver filter. Low- and high-energy images were corrected for scatter-veiling glare (5). The images were then logarithmically subtracted to form tissue-suppressed dual-energy images. An integrated iodine mass signal was obtained by summing all the background subtracted pixel values inside the region of interest for all the images. Control syringes containing blood drawn without contrast injection were used to subtract background blood signal from samples containing injected contrast material. The fraction of iodine recovered was determined from the ratio of collected iodine mass as quantified by dual energy logarithmic subtraction per injected iodine mass.

All pigs tolerated the procedure without complication. The removal of blood caused no significant hemodynamic compromise. Complete occlusion of the CS was confirmed under fluoroscopy by injecting contrast material distal to the inflated balloon. The analysis of the collected blood samples revealed that $50.6 \pm 12\%$ of the injected contrast material was removed from the CS.

Patients with underlying renal disease undergoing a CA are at high risk for CIN. It is well known that the amount of contrast material used in coronary interventions correlates with CIN (1,2). The major veins of the heart drain into the CS. By

using an occlusive balloon-tipped catheter in the ostium of the CS, we removed approximately 50% of the injected contrast in a swine model without complication. A pig's heart closely resembles a human's heart except for the presence of a large left azygos vein that empties into the CS (6,7). This anatomical shunt from the CS to the systemic circulation in pigs is most likely responsible for the lower-than-expected contrast removal in this study.

In humans, the connections to the systemic vein are minimal via ventricular thebesian veins (8). Therefore, it should be possible to remove most of the contrast from the CS before it enters the systemic circulation in humans, which may protect kidneys from CIN. However, anatomical variation of venous drainage of the heart is one of the limitations of this study for human use. The amount of blood lost during removal of contrast from the CS should be lower than 300 cc for conventional CA, which should be well tolerated. Access to the CS in humans can be obtained via the jugular vein without difficulty using currently available CS catheters with the addition of <30 min time to the procedure. The ability of our method to reduce CIN needs to be investigated by a randomized trial.

Using swine, despite an anatomical shunt from the CS to the systemic circulation via the azygos vein, we removed an average of $50.6 \pm 12\%$ of the injected contrast from the CS during CA. This study reports the first method for contrast removal during CA. Because the anatomical shunt from the CS to the systemic circulation is very small in humans, a higher yield of contrast removal from the CS can be expected for humans with the potential to reduce CIN.

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Please note: Dr. Movahed has a pending patent for a coronary sinus catheter for contrast removal.

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Letters to the Editor

Effects of N-3 Fatty Acids on Postoperative Atrial Fibrillation Following Coronary Artery Bypass Surgery

We read with considerable interest the recent contribution by Calò et al. (1) about the reduced incidence of postoperative atrial fibrillation (AF) after administration of n-3 polyunsaturated fatty acids (PUFAs) in patients undergoing coronary artery bypass surgery (CABG). Even though the investigators discuss the potential role of inflammation in this setting we consider that some important issues merit further clarification.

First, 19 of the studied patients were subjected to off-pump surgery, a procedure considered to be associated with a lesser oxidative and inflammatory response (2). Bearing in mind the hypothesis that postoperative AF may be reduced by off-pump CABG (3), it would be meaningful to examine whether there was a difference in the incidence of postoperative AF in this subset of patients.

In addition, it has been observed that the peak incidence of AF on the second or third postoperative day coincides with the peak of inflammatory markers such as C-reactive protein (CRP) and complement-CRP complexes (4). Recently, Abdelhadi et al. (5) confirmed this association, demonstrating a more pronounced and

prolonged increase in white blood cell counts of patients who developed postoperative AF. Thus, to validate the anti-inflammatory effects of PUFAs someone could investigate the variation of simple inflammatory indexes in the postoperative period. If Calò et al. have some available data on this issue it would be of interest to perform comparisons between the two groups.

Of note, more than one-half the total study population was taking statins perioperatively (1). Even though there were no differences regarding statin administration between the studied groups, the investigators could mention some data on potential differences in the incidence of postoperative AF within each group. Statins may exert beneficial pleiotropic effects on atrial remodeling, reducing the burden of the arrhythmia. It has also been indicated that statin therapy reduces the incidence of arrhythmias after CABG, although no specific data on AF was reported (6). Recently, Auer et al. (7) demonstrated a reduced incidence of AF after cardiac operation in patients receiving statins, but 44.7% of these had been subjected to valve surgery.

Accumulating evidence suggests that inflammation augments oxidative stress and vice versa, whereas oxidative stress seems to play an important role in atrial remodeling (2,8). Specifically, it has been shown that oral vitamin C administration significantly reduces the incidence of postoperative AF in CABG patients (8). Taking into account that PUFAs can attenuate oxidative stress in humans (9), it is reasonable to assume that their antioxidant action may contribute to their favorable effect on postoperative AF.

Finally, we concur with the view of Calò et al. that administration of PUFAs merits further evaluation in other forms of AF, but, as suggested by a recent study that reported no association between PUFA consumption from fish and the risk of AF (10), careful selection of the studied population should be performed.

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